

Amendment to the Claims:

Please amend the claims as follows:

Please cancel claims 14 to 26, 29 to 31, and 38, without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A transgenic mouse comprising:

a first transgenic nucleotide sequence, integrated into the genome of said mouse, comprising a sequence encoding a wild type or ~~751-amino acid isoform (hAPP751)~~ human amyloid precursor protein (hAPP) 751 amino acid isoform (hAPP751) operably linked to a first promoter; and

a second transgenic nucleotide sequence, integrated into the genome of said mouse, comprising a sequence encoding a wild type human (h) α -synuclein operably linked to a second promoter;

wherein the first and second transgenic nucleotide sequences are expressed, the first and the second promoter comprises a neuron-active promoter, and as a result of expression of the hAPP and (h) α -synuclein, said transgenic mouse develops amyloidosis, neurofibrillary tangles or intraneuronal accumulation of (h) α -synuclein.

Claim 2 (original): The transgenic mouse of claim 1, wherein said first promoter comprises a platelet-derived growth factor β (PDGF- β) promoter.

Claim 3 (original): The transgenic mouse of claim 2, wherein a simian virus (SV)40 derived intron operably links said PDGF- β promoter to said first transgenic nucleotide sequence.

Claim 4 (original): The transgenic mouse of claim 1, wherein said first promoter comprises a Thy1 promoter.

Claim 5 (original): The transgenic mouse of claim 1, wherein said first promoter comprises a prion (PrP) promoter.

Claim 6 (original): The transgenic mouse of claim 1, wherein said first promoter comprises a PDGF- β promoter.

Claim 7 (original): The transgenic mouse of claim 6, wherein a SV40 derived intron operably links said PDGF- β promoter to said second transgenic nucleotide sequence.

Claim 8 (original): The transgenic mouse of claim 1, wherein said second promoter comprises a Thyl promoter.

Claim 9 (original): The transgenic mouse of claim 1, wherein said second promoter comprises a PrP promoter.

Claim 10 (original): The transgenic mouse of claim 1, wherein said second promoter comprises a PDGF- β promoter.

Claim 11 (original): The transgenic mouse of claim 10, wherein a SV40 derived intron operably links said PDGF- β promoter to said second transgenic nucleotide sequence.

Claim 12 (previously presented): The transgenic mouse of claim 1, wherein proteins encoded by the first and second transgenic nucleotide sequences are overexpressed as compared to levels of equivalent proteins encoded by a non-transgenic mouse of the same strain.

Claim 13 (previously presented): The transgenic mouse of claim 1, wherein the nucleotide coding sequence of hAPP comprises an intron between exons 6 through 9 of the hAPP-encoding sequence.

Claims 14 to 26 (canceled)

Claim 27 (currently amended): A transgenic mouse comprising:

a first transgenic nucleotide sequence, integrated into the genome of said mouse, comprising a sequence encoding a wild-type human amyloid precursor protein (hAPP) 751 amino acid isoform (hAPP751) operably linked to a platelet derived growth factor β (PDGF- β) promoter operably linked to a simian virus (SV) 40 intron; and

a second transgenic nucleotide sequence, integrated into the genome of said mouse, comprising a sequence encoding a human (h) α -synuclein operably linked to a PDGF- β promoter operably linked to an SV40 intron;

wherein the first and second transgenic nucleotide sequences are expressed, and as a result of expression of the hAPP and (h) α -synuclein, said transgenic mouse develops amyloidosis, neurofibrillary tangles or intraneuronal accumulation of (h) α -synuclein.

Claim 28 (original): The transgenic mouse of claim 27, wherein proteins encoded by the first and second transgenic nucleotide sequences are overexpressed as compared to a non-transgenic mouse of the same strain.

Claims 29 to 31 (canceled)

Claim 32 (original): The transgenic mouse of claim 27, wherein neurodegenerative disease comprises formation of intraneuronal inclusions characteristic of Lewy body disease.

Claim 33 (original): The transgenic mouse of claim 27, wherein neurodegenerative disease comprises formation of fibrillary Lewy body-like inclusions.

Claim 34 (original): The transgenic mouse of claim 27, wherein neurodegenerative disease comprises neuronal death.

Claim 35 (original): The transgenic mouse of claim 27, wherein neurodegenerative disease comprises development of motor deficits.

Claim 36 (previously presented): The transgenic mouse of claim 27, wherein age of onset of the neurodegenerative disease occurs at a significantly ($p < 0.05$) younger age than in a singly transgenic (having only one of either the first or the second transgene) littermates.

Claim 37 (withdrawn - currently amended): A method for screening therapeutic agents for the prevention or treatment of neurological disease comprising administration of therapeutic interventions to ~~the [[a]] transgenic mouse of claim 1 or claim 27 comprising: a first transgenic nucleotide sequence, integrated into the genome of said mouse, encoding human amyloid precursor protein (hAPP) operably linked to a first promoter; a second transgenic nucleotide sequence, integrated into the genome of said mouse, encoding human (h) α -synuclein operably linked to a second promoter; wherein the first and second transgenic nucleotide sequences are expressed, the first and the second promoter comprises a neuron active promoter, and as a result of expression of the hAPP and (h) α -synuclein, said transgenic mouse develops amyloidosis, neurofibrillary tangles or intraneuronal accumulation of (h) α -synuclein.~~

Claim 38 (canceled)

Claim 39 (withdrawn - currently amended): A method for screening for an agent for the prevention or treatment of intraneuronal accumulation of α -synuclein, amyloidosis or neurofibrillary tangles, comprising

- (a) providing a potential therapeutic agent;
- (b) administering the potential therapeutic agent of (a) to the transgenic mouse of claim 1 or claim 27 ~~[[38]]~~; and
- (c) determining whether because of the administering of the potential therapeutic agent in (b) intraneuronal accumulation of α -synuclein, amyloidosis or neurofibrillary tangles in the transgenic mice is prevented or slowed.

Claim 40 (currently amended): A method of making a transgenic mouse comprising:

- (a) integrating into the genome of a mouse a sequence comprising a wild type human amyloid precursor protein (hAPP) 751 amino acid isoform hAPP751 ~~or a wild type human amyloid precursor protein (hAPP)~~ encoding nucleic acid operably linked to a first promoter; and
- (b) integrating into the genome of the mouse a sequence comprising a human (h) α -synuclein-encoding nucleic acid operably linked to a second promoter, wherein the first and the second promoter comprises a neuron-active promoter.

Claim 41 (currently amended): An inbred [[A]] transgenic mouse strain made by the method of claim 40.

Claim 42 (currently amended): An inbred [[A]] transgenic mouse strain made by propagating the mice of claim 41.

Claim 43 (currently amended): An inbred [[A]] transgenic mouse strain made by propagating the transgenic mice of claim 1.